PURIFICATION OF TAURINE-CONJUGATION-TYPE BILE ACID

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Applicant(s):: TOKYO TANABE CO LTD
Requested Patent: JP4169597
Application Number: JP19900291942 19901031
Priority Number(s):
IPC Classification: C07J9/00
EC Classification:
Equivalents: JP2011407C, JP7049438B

Abstract

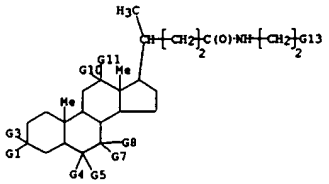
PURPOSE:To simply obtain the title bile acid of high purity by reaction of taurine with a bile acid followed by removing the organic solvent or unreacted raw materials and then by injecting the resulting aqueous solution into a column packed with e.g. ODS silica gel followed by elution with e.g. an organic solvent.
CONSTITUTION:A bile acid of formula I (R<1> to R<4> are each H, alpha- or beta-hydroxyl group which may carry a protecting group, or ketone) is reacted with taurine, and a liquor after reaction is feed from the organic solvent or unreacted raw materials, and the resulting aqueous solution is injected into a column packed with 2-20 times (v/w) reverse-phase synthetic resin or ODS silica gel based on the taurine-conjugation-type bile acid followed by elution with a water-soluble organic solvent (e.g. methanol) singly or its mixture with water, thus obtaining the objective compound of formula II (X is H or alkali metal).

L10 ANSWER 16 OF 22 MARPAT COPYRIGHT 2001 ACS
ACCESSION NUMBER: 118:22466 MARPAT
TITLE: Purification of taurine-conjugated cholic acid
INVENTOR(S): Kimura, Noriyuki; Mikami, Kazutoshi; Sekine, Tomio
PATENT ASSIGNEE(S): Tokyo Tanabe Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04169597	A2	19920617	JP 1990-291942	19901031
JP 07049438	B4	19950531		

AB Taurine-conjugated cholic acid derivs. [I; R1-R4 = H, (protected) OH, oxo; X = H, alk. metal], useful as hypolipemic agents and Ca-absorption accelerators (no data), were purified on column chromatog. by elution with org. solvents or org. solvent mixt. with H2O. Et2N was added to a soln. of ursodeoxycholic acid in dioxolane with stirring, ClCO2Et was added at 10.degree., followed by a soln. of taurine in 1N NaOH with stirring, the solvent was distd. in vacuo, til. HCl was added to pH 6, extd. with EtOAc the aq. phase was treated with NaOH and distd. in vacuo, the aq. phase then made neutral with dil. HCl and eluted on reverse-phase synthetic resins HP-21 with 50% MeOH to give 81.9% I (R1 = .alpha.-OH, R2 = R4 = H, R2 = .beta.-OH, X = Na) of >99.9% purity.

MSTR 2



L10 ANSWER 16 OF 22 MARPAT COPYRIGHT 2001 ACS (Continued)
G1 = OH
G4 = OH
MPL: claim 1

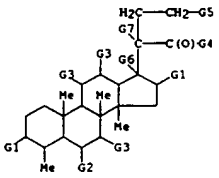
L10 ANSWER 17 OF 22 MARPAT COPYRIGHT 2001 ACS
ACCESSION NUMBER: 114:171313 MARPAT
TITLE: Pharmaceutical aerosol of polypeptide containing amphiphilic steroid as permeation enhancer
INVENTOR(S): Wang, Yu Chang John; Lee, William A.; Naroq, Blair
PATENT ASSIGNEE(S): California Biotechnology, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9009167	A1	19900823	WO 1990-US577	19900201
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
US 5011678	A	19910430	US 1989-305520	19890201
AU 9051594	A1	19900905	AU 1990-51594	19900201
PRIORITY APPLN. INFO.:			US 1989-305520	19890201
			WO 1990-US577	19900201

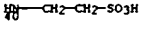
AB The title compns. comprise (1) a pharmaceutically active substance, e.g. a polypeptide; (2) a biocompatible steroid I [dashed line = single or double bond; D = group with mol. wt. <600 daltons which renders I water sol. at pH 2-12; E, G = OAc, OH, lower (hetero)alkyl; W = OAc, H; Q, V, X = OH, H]; and (3) a biocompatible (hydro/fluoro)carbon propellant. The steroid contains 2-3 polar functions exclusive of D and is capable of increasing the permeation of a human or animal mucosal surface by a pharmaceutically active substance. The propellant comprises e.g. .gtoreq.1 fluorocarbon CnHxClyFz (n = 1-4; x , y, z are such that x + y + z= 2n+2, y+z.gtoreq.2, and z > 0). Thus, an aerosol formulation was prepd. contg. Zn insulin, Na tauro-24,25-dihydrofusidate, CCl3F, and CCl2F2. When the compn. was administered intranasally to sheep, there was a 2.3 fold increase in bioavailability as compared to control formulation.

MSTR 1

L10 ANSWER 17 OF 22 MARPAT COPYRIGHT 2001 ACS (Continued)



G1 = OCOMe
G2 = OCOMe
G4 = 40



G5 = 36

MPL: claim 1